CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

21-016

CORRESPONDENCE

Groton Laboratories
Pfizer Inc
Eastern Point Road
Groton, CT 06340
Tel 860 441 4100

Global Research & Development

September 26, 2000

Russell Katz, M.D., Director
Division of Neuropharmacological Drug Products
Center for Drug Evaluation and Research HFD#120
Woodmont II Building
ATT. DOCUMENT CONTROL ROOM
1451 Rockville Pike
Rockville, MD 20852

Dear Dr. Katz:

RE: NDA 21-016 - Relpax™ (eletriptan hydrobromide) Oral

GENERAL CORRESPONDENCE

Reference is made to our New Drug Application submitted October 27, 1998 and to our Resubmission dated June 1, 2000. At this time we wish to update the patent information (Section 13 of New Drug Application) and marketing status.

Patent Information: The patent covering the eletriptan hydrobromide salt issued in the United States on August 29, 2000. This patent covers the proposed commercial tablet form of Relpax™. Particulars of the patent are as follows:

Patent No.:	6,110,940
Grant Date:	August 29, 2000
Expiration Date:	August 29, 2017
Application No.:	08/776,680
Application Date:	May 17, 1995

Foreign Marketing History: The following is a list of countries where the drug has been approved for marketing:

Austrailia	August 31, 2000
Brazil	July 25, 2000
Colombia	May 16, 2000
Czech Republic	May 10, 2000
Guatemala	June 6, 2000
Mexico	February 23, 2000
New Zealand	April 28, 2000
Venezuela	January 24, 2000

Product Labeling: [redacted]

If you have any questions, please do not hesitate to call me at (860) 715-2979.

Sincerely,

Larry Paglia

Larry M. Paglia, Ph.D.
Senior Associate Director
Regulatory Affairs Department

NDA ACTION LETTER ROUTING RECORD

NDA#: 021-016

Drug: Relpax (eletriptan)

Date Received: 10-26-99

Division: HFD- 120

Type of Letter: AP (AE) NA

Drug Classification: _____

Patent Info Received: ✓

Safety Update: Requested in ltr.

Phase IV Commitment: none

REVIEWER	RECEIPT	ACTION
Linda Carter Special Assistant to the Director	Date 10/27/99 Initials /S/	Date 10/27/99 Initials /S/

Comments: User Fee Goal date: October 27, 1999

Chemistry Review	Date 10.27.99 Initials /S/	Date 10.27.99 Initials /S/

Comments: EER ok NV pending. Labeling: /S/ sections to Description Section (nomenclature, strength); How Supplied (stability storage statement) should be made. According to Labeling this product will be marketed in blisters only

Pharmacology & Toxicology Review	Date 10/27/99 Initials /S/	Date 10/27/99 Initials /S/

Comments: Doses causing Segment II effects should be compared to humans based on AUC ratios, as was done in other data sections. Nursing mothers section should contain medical management advice as per 21 CFR 201.57(f)(8)(ii).

R. Temple, M.D. Director, Office of Drug Evaluation I	Date _____ Initials _____	Date _____ Initials _____ Returned to Division for Corrections _____ Forwarded _____

Comments:

Letter Signed _____

NDA 21-016

SEP 2 3 1999

Pfizer Inc.
Central Research Division
Attention: Nancy E. Martin
Eastern Point Road
Groton, CT 06340

Dear Ms. Martin:

Please refer to your new drug application (NDA) dated October 27, 1998, received October 27, 1998, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Relpax (eletriptan) 20 mg, 40 mg, 80 mg tablets.

We acknowledge receipt of your submissions dated the following:

Feburary 8, 1999	April 27, 1999	June 17, 1999
February 22, 1999	May 27, 1999	June 25, 1999
February 25, 1999	June 3, 1999	July 26, 1999
April 8, 1999	June 11, 1999	July 29, 1999.
April 20, 1999	June 15, 1999	

Finally, please refer to the teleconference held on August 26, 1999 between Drs. Cheryl Graham, Ashley Milton, Neville Jackson, and Ms. Nancy Martin of your firm and Drs. Robert Temple, Randy Levin of the Agency.

In addition to the issues discussed in the August 26, 1999 teleconference, we have the following comments regarding your application:

We noted that the peri- and postnatal study which was submitted to the NDA did not include an assessment of memory or learning in F1 pups. In response to our request of January 27, 1999 to conduct such a study, you informed us that the study was started on March 9, 1999. That study should be completed at this time, and we would like to assess the results prior to final approval.

We have also concluded, based on the lack of either reproductive or general toxicity, that the rat fertility study was conducted using doses (5, 15 and 50 mg/kg) that were too low to provide an adequate assessment of the potential effects of eletriptan on fertility. We note that you justified the dose selection based on a decreased body weight gain observed at 100 mg/kg in the rat embryo fetal development study and the thyroid follicular hypertrophy observed at 100 mg/kg in a 1 month general toxicity study. However, the latter effect does not define a maximally tolerated dose, and the body weight gain deficit observed in the embryofetal development study is probably specific to the pregnancy status of the females during dosing, as it did not occur in the 1 month general toxicology study. We therefore request that you repeat the study, exposing animals to appropriately high doses.

These comments are being provided to you prior to completion of our review of the application to give you preliminary notice of issues that have been identified. Per the user fee reauthorization agreements, these comments do not reflect a final decision on the information reviewed and should not be construed to do so. These comments are preliminary and are subject to change as the review of your application is finalized. In addition, we may identify other information that must be provided prior to approval of this application. If you choose to respond to the issues raised in this letter during this review cycle, depending on the timing of your response, as per the user fee reauthorization agreements, we may or may not be able to consider your response prior to taking an action on your application during this review cycle.

If you have any questions, contact Lana Chen, R.Ph., Regulatory Management Officer, at (301) 594-5529.

Sincerely,

/S/ 9/2-/99

Russell Katz, M.D.
Acting Director
Division of Neuropharmacological Drug Products
Office of Drug Evaluation I
Center for Drug Evaluation and Research

cc:
Archival NDA 21-016
HFD-120/Div. Files
HFD-120/L.Chen
HFD-120/Katz/Levin/Oliva/FITZGERALD /S/ 9/1/99 /S/ 9/1/99 /S/ 9/22/99
HFD-002/ORM
HFD-101/ADRA
HFD-95/DDMS 8.1.99
HFD-810/DNDC Division Director /S/ 8/31/99
HFD-860/Sahajwalla/Yuan
HFD-710/Jin/Flyer

DISTRICT OFFICE

Drafted by: lyc/August 5, 1999
Initialed by:
final:
filename:

INORMATION REQUEST

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

NDA 21-016

Pfizer Inc.
Attention: Nancy Martin
50 Pequot Avenue
New London, CT 06320

Dear Ms. Martin:

We acknowledge receipt on June 28, 2002 of your June 27, 2002 resubmission to your new drug application for Relpax (eletriptan) 20 mg, 40 mg, and 80 mg tablets.

We consider this a complete, class 2 response to our December 1, 2000 action letter. Therefore, the user fee goal date is December 28, 2002.

If you have any question, call Lana Chen, Regulatory Project Manager, at (301) 594-5529.

Sincerely,

{See appended electronic signature page}

John S. Purvis
Chief, Project Management Staff
Division of Neuropharmacological Drug Products
Office of Drug Evaluation 1
Center for Drug Evaluation and Research

This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.

/s/

Jack Purvis
9/17/02 10:59:45 AM

Central Research Division
Pfizer Inc
Eastern Point Road
Groton, CT 06340
Tel 860 441 4100

DESK COPY

Central Research

Department of Clinical Research

July 22, 1999

Russell Katz, M.D., Acting Director
Division of Neuropharmacological Drug Products
Center for Drug Evaluation and Research HFD #120
Office of Drug Evaluation I
ATT: DOCUMENT CONTROL ROOM
1451 Rockville Pike
Rockville, MD 20852

Dear Dr. Katz:

RE: NDA - 21-016 - RELPAX™ (eletriptan hydrobromide) Tablets

GENERAL CORRESPONDENCE

Reference is made to the RELPAX™ Patient Package Insert provided in the October 27,1998 submission of NDA 21-016 and to our July 19,1999 labeling conference call with Ms. Lana Chen and Dr. Armando Oliva.

As discussed with Ms. Chen and Dr. Oliva, the RELPAX™ Patient Package Insert has recently been revised to enhance patient comprehension. A review copy of the Patient Package Insert is provided in **Enclosure #1**. The intended commercial presentation is provided in **Enclosure #2**.

Please forward any questions which you may have regarding this submission to Ms. Nancy Martin at (860) 441-1904 (telephone) or (860) 441-0870 (facsimile).

Sincerely yours,

Amy E. Provencher

for Nancy E. Martin
Senior Associate Director
Regulatory Strategy & Registration

Desk Copy: Ms. Lana Chen
Dr. Armando Oliva
NDA Submission No. 023

Clear

NDA 21-016

Pfizer Inc.
Central Research Division
Attention: Nancy E. Martin
Eastern Point Road
Groton, CT 06340

JAN 27 1999

Dear Ms. Martin:

Please refer to your pending October 27, 1998 new drug application submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Relpax (Eletriptan) 20 mg, 40 mg, 80 mg Tablets.

We are reviewing the Pharmacology section(s) of your submission and have the following comments and information requests:

A preliminary review of NDA 21-016 for eletriptan indicates that in the peri- and post-natal rat study (no. 96016/17), learning and memory were not assessed in the F1 generation. For drugs developed to treat migraine, for which the patient population is largely women of child bearing potential, it is customary for learning and memory of F1 pups to be assessed. Therefore, this letter is provided to advise you that upon completion of the NDA review we will be seeking your commitment to assess learning and memory in the F1 generation. We encourage you to initiate the study prior to completion of the NDA review.

We would appreciate your prompt written response so we can continue our evaluation of your NDA.

These comments are being provided to you prior to completion of our review of the application to give you preliminary notice of issues that have been identified. Per the user fee reauthorization agreements, these comments do not reflect a final decision on the information reviewed and should not be construed to do so. These comments are preliminary and are subject to change as the review of your application is finalized. In addition, we may identify other information that must be provided prior to approval of this application. If you choose to respond to the issues raised in this letter during this review cycle, depending on the timing of your response, as per the user fee reauthorization agreements, we may or may not be able to consider your response prior to taking an action on your application during this review cycle.

NDA 21-016

If you have any questions, contact Lana Chen, R.Ph., Regulatory Management Officer, at (301) 594-5529.

Sincerely,

/S/ 1/22/99

Russell Katz, MD
Acting Director
Division of Neuropharmacological Drug Products
Office of Drug Evaluation I
Center for Drug Evaluation and Research

NDA 21-016

cc:
Archival NDA 21-016
HFD-120/Div. Files
HFD-120/Levin/Oliva
HFD-120/Fitzgerald/Chen
HFD-120/L.Chen
HFD-810/DNDC Division Director (only for CMC related issues)
DISTRICT OFFICE

1/19/99 /S/ 1/22/99 /S/ 1/22/99

Drafted by: lyc/January 14, 1999
Initialed by:
final:
filename: N21016PH.LT1

INFORMATION REQUEST (IR)

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Chen

Food and Drug Administration
Rockville MD 20857

NDA 21-016

Pfizer Inc.
Central Research Division
Attention: Nancy E. Martin
Eastern Point Road
Groton, CT 06340

DEC 24 1998

October 27, 1998

Dear Ms. Martin:

We have received your new drug application (NDA) submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for the following:

Name of Drug Product: Relpax (Eletriptan)

Therapeutic Classification: Standard

Date of Application: October 27, 1998

Date of Receipt: October 27, 1998

Our Reference Number: 21-016

Unless we notify you within 60 days of our receipt date that the application is not sufficiently complete to permit a substantive review, this application will be filed under section 505(b) of the Act on December 27, 1998 in accordance with 21 CFR 314.101(a).

Under 21 CFR 314.102© of the new drug regulations, you may request an informal conference with this Division (to be held approximately 90 days from the above receipt date) for a brief report on the status of the review but not on the application's ultimate approvability. Alternatively, you may choose to receive such a report by telephone. Should you wish a conference, a telephone report, or if you have any questions concerning this NDA, please contact Lana Chen, R.Ph., Regulatory Management Officer, at (301) 594-5529.

Please cite the NDA number listed above at the top of the first page of any communications concerning this application.

Sincerely yours,

/S/ 12/23/98

Paul Leber, M.D.
Director
Division of Neuropharmacological Drug Products
Office of Drug Evaluation I
Center for Drug Evaluation and Research

cc:
Original NDA 21-016
HFD-120/Div. Files
HFD-120/CSO/L.Chen
HFD-120/R.Levin RL 12/16/98
DISTRICT OFFICE

Drafted by: lyc 12/3/98
Final: 12/3/98

ACKNOWLEDGEMENT (AC)

USAN

UNITED STATES ADOPTED NAMES COUNCIL

SOPHIA V. FUERST, Associate Secretary
(312) 464-5352

American Medical Association
515 North State Street
Chicago, Illinois 60610

Telefax: 312-464-4184
E-mail: Sophia_Fuerst@ama-assn.org

September 24, 1997

JJ-101

Pfizer Inc.
Central Research Division
Eastern Point Road
Groton, CT 06340

Attn: Jasjit S. Bindra, PhD
Senior Science Advisor

Dear Dr. Bindra:

It is my pleasure to inform you that the USAN Council adopted **eletriptan hydrobrimide** as the United States Adopted Name for UK-116,004-04, Pfizer Inc.'s $5HT_{1D}$-serotonin receptor agonist used in the treatment of migraine.

Enclosed is a copy of the Statement of Adoption on **eletriptan hydrobromide**. I plan to schedule publication of this information in the journal of *Clinical Pharmacology and Therapeutics* unless you request a delay within the next thirty days. Please use the enclosed statement to provide comments or additions. If this information is accurate, and may be published, please initial the statement and return it to me.

Sincerely yours,

Sophia V. Fuerst
Assistant Secretary
USAN Council

SVF

Enclosure: N97;76

N97
76

September 24, 1997

STATEMENT ON A NONPROPRIETARY NAME ADOPTED BY THE USAN COUNCIL:

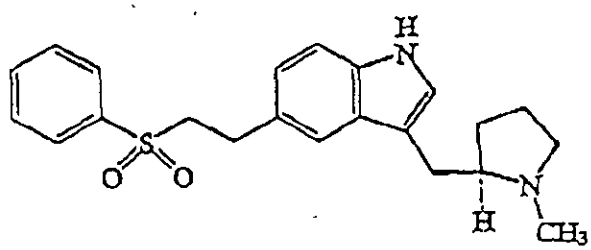
USAN (JJ-101)	ELETRIPTAN HYDROBROMIDE
PRONUNCIATION	el e trip' tan
THERAPEUTIC CLAIM	antimigraine ($5HT_{1D}$-serotonin receptor agonist)

CHEMICAL NAMES

(1) (*R*)-3-[(1-methyl-2-pyrrolidinyl)methyl]-5-[2-(phenylsulfonyl)ethyl]-1*H*-indole monohydrobromide

(2) 3-[[(*R*)-1-methyl-2-pyrrolidinyl]methyl]-5-[2-(phenylsulfonyl)ethyl]indole, monohydrobromide

STRUCTURAL FORMULA



· HBr

MOLECULAR FORMULA	$C_{22}H_{26}N_2O_2S$ · HBr
MOLECULAR WEIGHT	463.4
TRADEMARK	Unknown as yet
MANUFACTURER	Pfizer Inc.
CODE DESIGNATION	UK-116,044-04
CAS REGISTRY NUMBER	177834-92-3
WHO NUMBER	7426

SF